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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------|------------------|
| 09/869,796 | 09/19/2001 | Eric DeFranco | 110024 | 1327 |
| 25944 | 7590 | 06/15/2004 | EXAMINER | |
| OLIFF & BERRIDGE, PLC P.O. BOX 19928 ALEXANDRIA, VA 22320 | | | LEWIS, PATRICK T | |
| | | | ART UNIT | PAPER NUMBER |

1623

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|--------------------------------------|--|--|
| Office Action Summary | Application No. 09/869,796 | Applicant(s) DEFRANCO ET AL. | |
| | Examiner Patrick T. Lewis | Art Unit 1623 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 6-16, 18-27, 29 and 30 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 6, 7, 9-16, 22-27, 29 and 30 is/are rejected.
- 7) ☒ Claim(s) 8 and 18-21 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's Response dated March 11, 2004

1. In the Response filed March 11, 2004, claims 1 and 13 were amended; claims 5, 17, and 28 were canceled; and claims 29-30 were added.
2. Claims 1-4, 6-16, 18-27, and 29-30 are pending. An action on the merits of claims 1-4, 6-16, 18-27, and 29-30 is contained herein below.
3. The rejection of claims 1-28 under 35 U.S.C. § 112, second paragraph, has been rendered moot in view of applicant's amendment dated March 11, 2004.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-4, 10-16, 22-27, and 29-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "optionally carrying one or more modifications on one of the constituent elements of said nucleotide or nucleoside" as recited in independent claims 1 and 13 renders said claims and subsequent dependent claims indefinite. In the absence of distinct modifications to the chemical core claimed or distinct language to describe the structural modifications or the chemical names of modified compounds of this invention, the identity of said modified compounds

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would be difficult to describe and the metes and bounds of said modified compounds applicant regards as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated in the claims.

6. Claim 11 recites the limitation "the chemical and/or enzymatic route" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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9. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 1-2, 6-7, and 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Bergstrom et al. *J. Org. Chem.* (1981), Vol. 46, pages 1432-1441 (Bergstrom) and Dellinger et al. US 6,555,030 (Dellinger).

Claim 1 is drawn to functionalized compound of general formula (I). Claims 2, 6-7, and 9-12 depend claim 1. Claim 2 limits R₁ to an alkyl having at most 6 carbon atoms. Claim 6 limits W to the general formula (II). Claims 7 and 9 depend from claim 6. Claim 6 limits the nitrogen-containing base. Claim 9 limits R₂, R₃, and R₄. Claim 10 is drawn to a polynucleotide comprising at least one functionalized compound according to claim 1. Claim 11 limits the polynucleotide of claim 10 to those prepared by chemical and/or enzymatic route. Claim 12 further limits claim 11 to a polynucleotide prepared using an enzymatic reaction.

Bergstrom teaches C-5 substituted pyrimidine nucleosides. Specifically, Bergstrom teaches 5-(4-methyl-3-oxopentyl)-2'-deoxyuridine (compound 20, Table II, page 1437). The purpose of the study was to lay the groundwork and establish methodology for attaching functionalized side chains to the C-5

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positions of pyrimidine and pyrrolo-[2,3-*d*]pyrimidine nucleosides (Conclusion, pages 1438). Modification at the nucleoside, nucleotide, and polynucleotide level could produce a wide array of useful nucleic acid-base-derived biological probes.

The instantly claimed invention differs from Bergstrom in that Bergstrom does not explicitly teach a compound of formula (I) wherein L comprises at least 4 atoms. Bergstrom does not explicitly teach a compound wherein W corresponds to the general formula (II) wherein R₂ is a 2-cyanoethyl-N,N-diisopropylphosphoramidite group and R₄ is a 4,4-dimethoxytrityl group. Bergstrom also does not explicitly teach compound incorporated into a polynucleotide.

Dellinger teaches a conventional 3'-to-5' oligonucleotide synthesis using DMT as a 5'-OH protecting group (Figure 1). As illustrated in Figure 1, compounds containing a 3'-phosphoramidite wherein 5'-OH is protected with DMT are routinely employed in the synthesis of oligonucleotides and polynucleotides.

It would have been obvious to one of ordinary skill in the art at the time of the invention produce compounds of general formula (I) wherein L is comprised of at least four atoms. Compound **20** is a homologue of the instantly claimed compound of formula (I) wherein the difference between the compounds is the length of the linker arm (differs by one methylene unit). Compound **20** and the instantly claimed compound have very close structural similarities and similar utilities. An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed

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compound. Although not exemplified, Bergstrom clearly suggests the use of the C-5 substituted pyrimidine nucleosides incorporated into polynucleotides. It would have been obvious to one of ordinary skill in the art at the time of the invention to produce such a polynucleotide using well-known conventional methods as taught by Dellinger. One of ordinary skill would have been motivated to do so in order to produce nucleic acid-base-derived biological probes.

Conclusion

11. Claims 1-4, 6-16, 18-27, and 29-30 are pending. Claims 1-4, 6-7, 9-16, 22-27, and 29-30 are rejected. Claims 8 and 18-21 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. No claims are allowed.

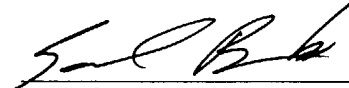
Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on M-F 10:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patrick T. Lewis, PhD
Examiner
Art Unit 1623



Dr. Samuel Barts
Primary Patent Examiner
Technology Center 1600

ptl
June 9, 2004